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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/542,914	03/07/2006	Alfred Marchal	09997.0127USWO	9556

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EXAMINER	
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ART UNIT	PAPER NUMBER
1621	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/542,914	MARCHAL, ALFRED	
	Examiner	Art Unit	
	Jennifer Y. Cho	1621	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/31/07 has been entered.

Claims 1 and 3-10 are pending in this application. Claims 2 and 11-17 have been cancelled.

Response to Arguments

Applicant's arguments are moot in view of the new grounds of rejection.

Claim Objections

Claim 1 is objected to because of the following informalities: The bonding structure for formula I is incorrect. The bridgehead carbons on the epoxide ring have an extra double bond. These two carbons are hypervalent, each with five bonds. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 3 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

The nature of the invention

The nature of the invention is directed to the use of compounds of formula I for the preparation of pharmaceutical or cosmetic composition(s) that can be used for the treatment of dermatological lesions, consisting of bruises, vascular disorders on the skin, spider veins, varicoses, blotches on the face, purpura on the face, body or legs, irritation following use of chemical peel, Schamberg's disease or a mixture thereof.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that the pharmacological art involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat dermatological lesions). There is no absolute predictability even in view of the seemingly high level of skill in the art.

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In the instant case, the specification shows how Vitamin K1 oxide is suitable for the treatment of bruises, but not for all dermatological lesions, including vascular disorders on the skin, spider veins, varicoses, blotches on the face, purpura on the face, body or legs, irritation following use of chemical peel, Schamberg's disease. There is

no conclusive data directed to these treatments in Applicant's specification or in the 1.132 Declaration filed on 4/10/07.

Thus, the specification does not provide guidance as to how one skilled in the art would accomplish the objective of treating dermatological lesions as a general class consisting of disorders on the skin, spider veins, varicoses, blotches on the face, purpura on the face, body or legs, irritation following use of chemical peel, Schamberg's disease. Nor is there any guidance provided as to a specific protocol to be utilized in order to show the efficacy of the presently claimed active ingredients for treating these dermatological lesions.

Specifically, it is highly unlikely, and the Office would require experimental evidence to support the contention that the claims specified could treat dermatological lesions by simply administering, by any method, a therapeutically active amount of the claim specified agents. The specification fails to enable one of ordinary skill in the art to practice the presently claimed method for treating these dermatological lesions.

Applicants have not provided any competent evidence or disclosed test results for the pharmaceutical use of treating any dermatological lesion for a human being or other mammal. Note that dermatological lesions could include skin cancer, acne and moles. No conclusive test results are disclosed in the specification that give guidance as to the actual effect of the compound on any mammal for dermatological lesions consisting of vascular disorders on the skin, spider veins, varicoses, blotches on the face, purpura on the face, body or legs, irritation following use of chemical peel, Schamberg's disease.

The amount of direction or guidance present and the presence or absence of working examples

The specification fails to provide any examples of the effect of the compound on mammals with dermatological lesions consisting of vascular disorders on the skin, spider veins, varicoses, blotches on the face, purpura on the face, body or legs, irritation following use of chemical peel, Schamberg's disease. It fails to provide test results to substantiate the use of a compound of formula I to treat these lesions.

The breadth of the claims

The instant breadth of the rejected claims is broader than the disclosure, specifically, the instant claims include treatment of vascular disorders on the skin, spider veins, varicoses, blotches on the face, purpura on the face, body or legs, irritation following use of chemical peel, Schamberg's disease or a mixture thereof, but the specification does not provide conclusive evidence of the effect of any of the claimed compounds on these dermatological lesions.

The quantity or experimentation needed and the level of skill in the art

It would require undue experimentation of one of ordinary skill in the art to ascertain the effectiveness of the compound in the treatment of dermatological lesions consisting of vascular disorders on the skin, spider veins, varicoses, blotches on the face, purpura on the face, body or legs, irritation following use of chemical peel,

Schamberg's disease. Factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant claims. The present state of the art is that studies on dermatological lesions are still being conducted. There is a lack of convincing and substantial evidence linking Vitamin K1 oxide to treatment of dermatological lesions consisting of vascular disorders on the skin, spider veins, varicoses, blotches on the face, purpura on the face, body or legs, irritation following use of chemical peel, Schamberg's disease. In view of the breadth of the claims, the chemical nature of the invention and unpredictability of treating dermatological lesions consisting of vascular disorders on the skin, spider veins, varicoses, blotches on the face, purpura on the face, body or legs, irritation following use of chemical peel, Schamberg's disease. and the lack of working examples regarding the activity as claimed, one skilled in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in cope with the claims.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001, states that " a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

In consideration of the Wand factors, it is apparent that undue experimentation because of variability in prediction of outcome that is not addressed by the present application disclosure, examples, teaching and guidance presented. Absent factual

data to the contrary, the amount and level of experimentation needed is undue.

Therefore, claims 1 and 3 are rejected under 35 U.S.C. § 112, 1st paragraph.

Claim Rejections – 35 USC 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

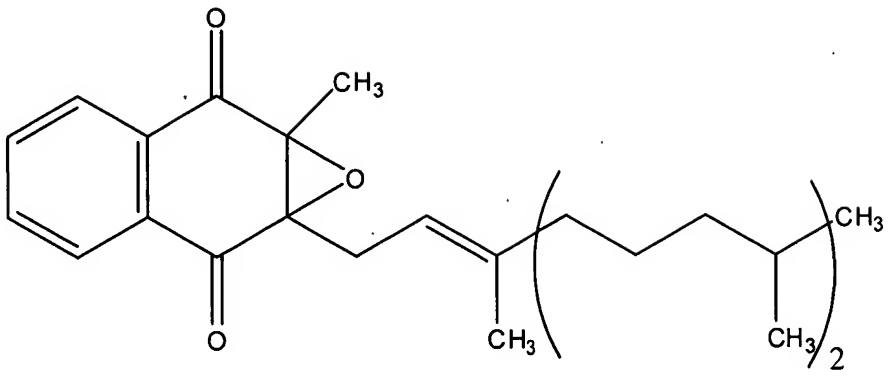
> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1 and 3-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Elson (U.S. Patent 5,510,391), in view of Ryall et al. (J. Med. Chem. 1990 (33), 1790-1797).

The instant claims are drawn to a method of treating dermatological lesions of a mammal by using a compound of formula I, as depicted below:



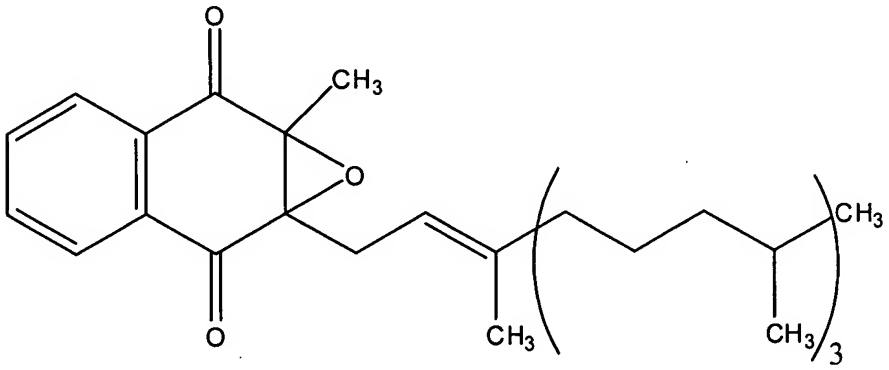
Elson teaches that synthetic Vitamin K1 analogs can be used in cosmetic and/or pharmaceutical formulation for use in treating the skin (see column 7, lines 18-20; abstract), as a cream (column 3, line 19-21) at concentrations of 1% and 5% (column 3, lines 40 and 55). Vitamin K1 oxide would be considered to be a species of the generic teaching of Elson. Elson's formulations treats blood vessel disorders of the skin, including actinic and iatrogenic purpura, lentigines, telangiectasias of the face, spider angiomas, spider veins of the face, spider veins of the legs and other vascular problems of the skin and subcutaneous tissue (column 1, lines 24-31). Additionally, Elson's formulations contain lecithin granules which are composed of lipid particles (abstract).

Regarding claims 4, 5 and 8 which presents limitations as to the particle size of the phospholipids and the percentage of the compound of Formula 1, it is the position of the examiner that one of ordinary skill in the art, at the time of the invention, would through routine and normal experimentation determine the optimization of these limitations to provide the best effective variable depending on the results desired. Thus it would be obvious in the optimization process to optimize the particle size of the

phospholipids and the percentage of the compounds. Note that the prior art provides the same effect desired by applicant, the treatment of the same skin conditions.

Elson is deficient in that it does not explicitly teach Vitamin K1 epoxide analogs.

Ryall et al. teaches Vitamin K1 epoxide analogs, including a homolog to that of Applicant's, differing only by one repeating isoprene unit., as shown below (page 1791, first column, compound 1, compound 2, second column, table 1, Vitamin K epoxide, first compound).



Additionally, Ryall et al.'s compounds are found to be inhibitors of Vitamin K1 epoxide reductase (page 1790, second column, first paragraph to page 1791, first column, first paragraph). The Examiner takes the position that it is reasonable to assume the mechanism of action for Applicant's Vitamin K1 epoxide compound also involves the inhibition of Vitamin K1 epoxide reductase, as taught by Ryall et al. Ryall et al. is analogous art because compounds of the same structural formula that differ only by one repeating unit would be obvious. Thus, varying Ryall et al.'s

compounds by one homologous isoprene unit, would give rise to the compound of the instant claims. In the absence of unexpected results, one skilled in the art would expect that the instant claims, directed to a compound that is homologous to the compounds of Ryall et al. are prima facie obvious.

Therefore, it is the position of the examiner that one of ordinary skill in the art, at the time of the invention, would through routine and normal experimentation determine the appropriate number of isoprene units in the side chain of the synthetic Vitamin K1 epoxide, as taught by Ryall et al. In addition, one of ordinary skill in the art would use these Vitamin K1 analogs in cosmetic and/or pharmaceutical formulation for use in treating the skin, as taught by Elson. Slight variations in the length of the side chain of Vitamin K1 epoxide suggests the compounds have similar properties and utilities. "Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties." (see MPEP § 2144.08c).

One of ordinary skill in the art would be motivated to use Ryall et al.'s compounds for Elson's formulations, with the reasonable expectation that the compounds would treat dermatological conditions involving blood vessel disorders, by inhibiting Vitamin K1 epoxide reductase. Furthermore, the limitations in some of the dependent claims, not expressly taught in the art, are also deemed to be obvious. One of ordinary skill in the art would be motivated to tweak and optimize these parameters to arrive at the instantly

claimed invention. The expected result would be the efficient production of Applicant's synthetic Vitamin K1 epoxide analog for the pharmaceutical and cosmetic industry.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Y. Cho whose telephone number is (571) 272 6246. The examiner can normally be reached on 9 AM - 6 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (571) 272 0871. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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